

The listing of claims will replace all prior versions, and listings, of claims in the application:

1-43. (cancelled)

44. (Previously Presented) An agent for inhibiting at least one of release, maturation and replication of a member of the Flaviviridae family selected from Flavivirus or Pestivirus and Hepacivirus-wherein the agent comprises, as an active component, at least one proteasome inhibitor in a pharmaceutical preparation.

45. (Previously Presented) An agent as claimed in claim 44, wherein the agent is used for the treatment and prophylaxis of HCV-induced hepatitis, flavivirus-induced fever, hemorrhages, leukopenia, thrombocytopenia, diarrheal diseases encephalitis or pestivirus-induced diseases.

46. (Previously Presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is a substance which inhibits, regulates or otherwise affects the activities of the ubiquitin/proteasome pathway; which specifically affects the enzymic activities of the complete 26S proteasome complex; and which specifically affects the enzymic activities of the free 20S, catalytically active, proteasome complex, which is not assembled with regulatory subunits.

47. (Previously Presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is taken up by higher eukaryotic cells and, after having been taken up into a cell, interacts with the catalytic subunits of the proteasome, and, in connection with this, blocks at least some of the proteolytic activities of the proteasome within the 26S or the 20S proteasome complex.

48. (Previously Presented) An agent as claimed in claim 45, wherein in addition to proteasome inhibitors, the pharmaceutical preparation also comprises at least one further agent which affects, regulates or inhibits the cellular ubiquitin system, such as the activities of the ubiquitin-conjugating enzymes and/or of the ubiquitin-hydrolyzing enzymes.

49. (Previously Presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is administered in various forms *in vivo*, i.e. orally, intravenously, intramuscularly, subcutaneously or in encapsulated form, with or without cell specificity-carrying changes, which, due to using a particular administration and/or dose regime, exhibit low cytotoxicity, which do not elicit any side effects, or only elicit insignificant side effects, and which exhibit a relatively high metabolic half life and a relatively low clearance rate in the body.

50. (Previously Presented) An agent as claimed in claim 45, wherein the proteasome inhibitor

- a) is isolated in natural form from microorganisms or other natural sources; or
- b) is formed from natural substances as a result of chemical modifications; or
- c) is prepared completely synthetically; or
- d) is synthesized *in vivo* using gene therapy methods.

51. (Previously Presented) An agent as claimed in claim 50, wherein the proteasome inhibitor belongs to the following substance classes:

- a) naturally occurring proteasome inhibitors:
 - peptide derivatives which contain epoxyketone structures C-terminally,

- β -lactone derivatives,
 - aclacinomycin A (also termed aclarubicin),
 - lactacystin and its chemically modified variants, such as the cell membrane-penetrating variant "clastolactacystein β -lactone"
- b) synthetically prepared proteasome inhibitors:
- modified peptide aldehydes, such as N-carbobenzoxy-L-leucinyl-L-leucinyl-L-leucinal (also designated MG132 or zLLL), its boric acid derivative MG232; N-carbobenzoxy-Leu-Leu-Nva-H (designated MG115; N-acetyl-L-leucinyl-L-leucinyl-L-norleucinal (designated LLnL) and N-carbobenzoxy-Ile-Glu(OBut)-Ala-Leu-H (also designated PSI);
- c) peptides which carry an α,β -epoxy ketone structure C-terminally, and also vinylsulfones, such as carbobenzoxy-L-leucinyl-L-leucinyl-L-leucinevinylsulfone, or 4-hydroxy-5-iodo-3-nitrophenylacetyl-L-leucinyl-L-leucinyl-L-leucinevinylsulfone (NLVS)
- d) glyoxylic acid or boric acid radicals, such as pyrazyl-CONH(CHPhe)CONH(CHisobutyl)B(OH)₂) and also dipeptidyl boric acid derivatives, or
- e) pinacol esters, such as benzyloxycarbonyl(Cbz)-Leu-Leu-boroLeu pinacol ester.

52. (Previously Presented) An agent as claimed in claim 50 wherein the particularly suitable proteasome inhibitor is the epoxyketone epoxomicin (epoxomycin, molecular formula:

C₂₈H₈₆N₄O₇) and/or eponemicin (eponemycin, molecular formula: C₂₀H₃₆N₂O₅).

53. (Previously Presented) An agent as claimed in claim 50 wherein the particularly suitable proteasome inhibitor is selected from the PS series

- a) PS-519 as β -lactone, and also as lactacystin derivative the compound IR-[1S,4R,5S]-1-(1-hydroxy-2-methylpropyl)-4-propyl-6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione - molecular formula $C_{12}H_{19}NO_4$ - and/or
- b) PS-341 as peptidyl-boric acid derivative the compound N-pyrazinecarbonyl-L-phenylalanine-L-leucine-boric acid - molecular formula $C_{19}H_{25}BN_4O_4$ - and/or
- c) PS-273 (morpholine-CONH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)₂) and its enantiomer PS-293 and/or
- d) compound PS-296 (8-quinolylsulfonyl-CONH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)₂) and/or
- e) PS-303 (NH₂(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)₂) and/or
- f) PS-321 as (morpholine-CONH-(CH-naphthyl)-CONH-(CH-phenylalanine)-B(OH)₂); - and/or
- g) PS-334 (CH₃-NH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)₂) and/or
- h) the compound PS-325 (2-quinol-CONH-(CH-*homo*-phenylalanine)-CONH-(CH-isobutyl)-B(OH)₂) and/or
- i) PS-352 (phenylalanine-CH₂-CH₂-CONH-(CH-phenylalanine)-CONH-(CH-isobutyl)-B(OH)₂) and/or

j) PS-383 (pyridyl-CONH-(CH₂F-phenylalanine)-CONH-(CH-isobutyl)-B(OH)₂).

54. (Previously Presented) A method of inhibiting at least one of the entry/internalization process, the replication and the maturation and release of Flaviviridae with the agent of claim 44.

55. (withdrawn) The method of claim 54, wherein the proteasome inhibitor inhibits late processes in the Flaviviridae life cycle.

56. (withdrawn) The method of claim 54, wherein the proteasome inhibitor blocks to a large extent or completely prevent the production of infectious virions from Flaviviridae-infected cells.

57. (withdrawn) The method of claim 54, wherein the proteasome inhibitor causes inhibition of the release of virions and also reduces the infectivity of the virions which are released.

58. (withdrawn) The method of claim 54, wherein the proteasome inhibitor suppresses virus replication and thus the spread of an infection *in vivo*.

59. (withdrawn) The method of claim 54, wherein the proteasome inhibitor inhibits the replication of Flaviviridae in accordance with the following mechanisms

- a) blocking/reducing the release of new virions;
- b) blocking/reducing the infectivity of released virions;
- c) blocking/reducing the spread of infection in cultures of host cells;
- d) blocking/reducing the spread of infection in infected organs *in vivo*.

60. (withdrawn) The method of claim 54, wherein the proteasome inhibitor suppresses flavivirus infections and pestivirus infections in humans and animals.

61. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for inducing the death of hepatocarcinoma cells.

62. (withdrawn) The use of proteasome inhibitors as claimed in claim 61 for suppressing and/or preventing the development of liver cell carcinomas.

63. (withdrawn) The use of proteasome inhibitors as claimed in claim 62 for treating patients who have established liver cell carcinomas.

64. (withdrawn) The use of proteasome inhibitors as claimed in claim 61 for treating/controlling/preventing HCV-induced liver cirrhosis and/or HCV-induced liver cell carcinomas, medicament-induced liver carcinomas, genetically determined liver carcinomas, environmentally determined liver carcinomas and/or liver carcinomas which are determined by a combination of viral and nonviral factors.

65. (withdrawn) The use of proteasome inhibitors as claimed in claim 61 for selectively eliminating liver carcinoma cells which develop as the result of a HCV infection, or a corresponding coinfection with HCV and hepatitis B virus (HBV), or a hepatitis delta virus (HDV)/HBV/HCV coinfection, human immunodeficiency virus (HIV)/HCV coinfections, or HCV and coinfections with other viruses, bacteria or parasites.

66. (withdrawn) The use of proteasome inhibitors as claimed in claim 61 for preventing the development, growth and metastasis of liver cell tumors and for preferentially destroying liver carcinoma cells in HCV-infected patients.

67. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for modulating the expression, modification and activity of the tumor suppressor protein p53 and other tumor suppressor proteins which are of importance in connection with hepatocellular carcinomas (HCCs).

68. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for liver cell regeneration in patients suffering from hepatitis.

69. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for regenerating patients following flavivirus infections.

70. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for regenerating stabled animals following flavivirus or pestivirus infections.

71. (withdrawn) The use of proteasome inhibitors as claimed in claim 54 for reducing the number of infected virus-producing cells in liver cell tissue.

72. (withdrawn) The method of claim 54, wherein the proteasome inhibitor alters the post-translational modification and proteolytic processing of Flaviviridae structural proteins and reduce the ability of the virus envelope proteins to dimerize and thereby reduce or block the release and infectivity of Flaviviridae.

73. (withdrawn) The method of claim 54, wherein the proteasome inhibitor inhibits both the maintenance and persistence of a previously established infection and of a secondary infection including blocking the spread of a Flaviviridae infection in vivo.

74. (withdrawn) A method of treating and controlling HCV-induced hepatitis, flavivirus-induced fever, hemorrhages and encephalitis and pestivirus-induced diseases with the agent of claim 50, wherein the agent comprises a combination of proteasome inhibitors.

75. (withdrawn) The method of claim 74, wherein the combination further comprises therapeutic agents which are already used in the antiviral therapy of Flaviviridae infections.

76. (withdrawn) The method of claim 74, wherein the combination is administered to treat coinfections with different flaviviruses and pestiviruses.

77. (withdrawn) The method of claim 74, wherein the combination is administered to treat coinfections of HCV and immunodeficiency viruses HIV-1 and HIV-2.

78. (withdrawn) The method of claim 77, wherein the combination is administered to treat HCV/HIV coinfections in combination with HAART therapy.

79. (withdrawn) The method of claim 54, wherein the proteasome inhibitor prevents a reinfection with HCV in connection with liver transplantations and other organ transplantations.

80. (withdrawn) The method of claim 54, wherein the proteasome inhibitor prevents a reinfection with HCV in connection with cell therapies, by administering the agents before, during and after the transplantation.

81. (withdrawn) The method of claim 54, wherein the proteasome inhibitor prevents a reinfection with HCV in connection with the transplantation of virus-free organs to chronic virus carriers who still possess residual virus and can infect new organs and also in connection with the transfer of virus-containing organs from donors to virus-free patients.

82. (withdrawn) The method of claim 54, wherein the proteasome inhibitor prevents the establishment of a systemic Flaviviridae infection immediately following contact with infectious virus.

83. (withdrawn) The method of claim 54, wherein the proteasome prevents a Flaviviridae infection in individuals who are at a high risk of fresh infection.

84. (withdrawn) The method of claim 54, wherein the proteasome decreases or eliminates a hepatitis by means of immune system-mediated mechanisms.

85. (withdrawn) A method of producing agents and/or pharmaceutical preparations for inhibiting the release, maturation and replication of Flaviviridae with at least one proteasome inhibitor, wherein the agent is the agent of Claim 50.

86. (withdrawn) The method of claim 85, wherein the agent comprises at least one proteasome inhibitor for producing pharmaceuticals for the treatment and prophylaxis of HCV-induced hepatitis, flavivirus-induced fever, hemorrhages and encephalitis and pestivirus-induced diseases.